

Applicant's arguments with respect to claims 1-23, 46, and 56-58 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1-23, 46, and 56-58 are pending.

Claims 1-23 are rejected.

Claims 46, and 56-58 are withdrawn from consideration.

#### **DETAILED ACTION**

1. Claims 1-23 are under consideration in this Office Action.

#### **Priority**

2. It is noted that this application is a division of 10/243,731 filed on 09/16/2002, which is a continuation of 09/489,157 filed on 01/21/2000(US 6,465,513), which claims benefit of 60/116,735 filed on 01/22/1999, and claims benefit of 60/117,743 filed on 01/29/1999 .

#### **Drawings**

3. None.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making hydrates of the claimed compounds. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. “The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims”, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed hydrate, the lack of predictability in the art, and the broad scope of the claims.

c) There is no working example of any hydrate formed. The claims are drawn to solvates, yet the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v.*

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*Cardinal Chemical Co.*, 28 USPQ2d 1190 “The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist.” The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

g) The state of the art is that is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). West, Anthony R., "Solid State Chemistry and its Applications, Wiley, New York, 1988, pages 358 & 365. The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, “it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent”. Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with

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polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stable region of the solvate.

h) The breadth of the claims includes all of the hundreds of thousands of compounds of claimed compound containing "a hydrate". Thus, the scope is broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 13, and 14, the term "containing" is recited. These expressions are vague and indefinite because the term "containing" would mean that there were some additional components present in addition to the ones recited. The claims do not specify what other additional components are. Therefore, an appropriate correction is required.

***Claim Rejections - 35 USC § 102***

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

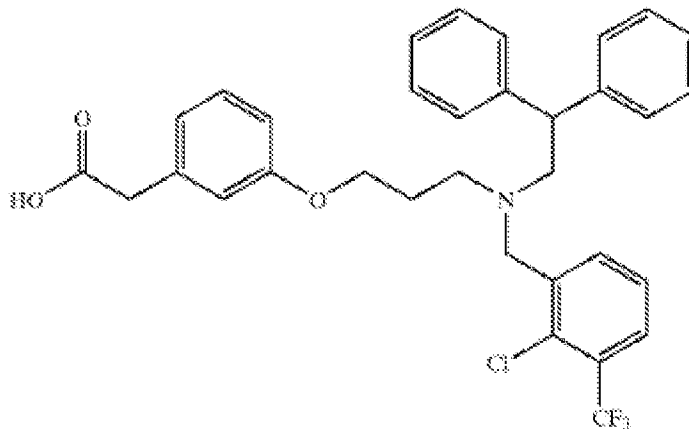
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 9- 21, and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Collins et al (US 2004/0072868).

Collins et al discloses the following compound as shown below (see col. 18, ex. 16):

EXAMPLE 16

[0315] 2-(3-{3-[[2-Chloro-3-(trifluoromethyl)benzyl](2,2-diphenylethyl)amino]propoxy}-phenyl)acetic Acid

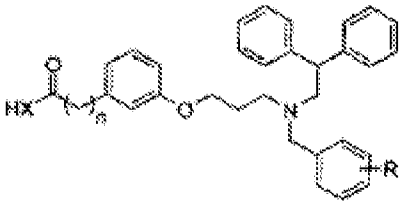


This is identical with the claims.

Claims 1-7, 9- 21, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins et al (J. Med. Chem. 2002, 45, 1963-1966).

Collins et al discloses the following compound as shown below (see page 1964, Table 1 ):

**Table 1. LXR Activity of Tertiary Amines<sup>a</sup>**



compd	n	X	R	EC <sub>50</sub> (nM)	RE	EC <sub>50</sub> (nM)	RE
12	1	O	2-chloro-3-(trifluoro- methyl)	125 ± 20	1.0	190 ± 30	1.7

This is identical with the claims.

### ***Claim Rejections - 35 USC § 103***

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

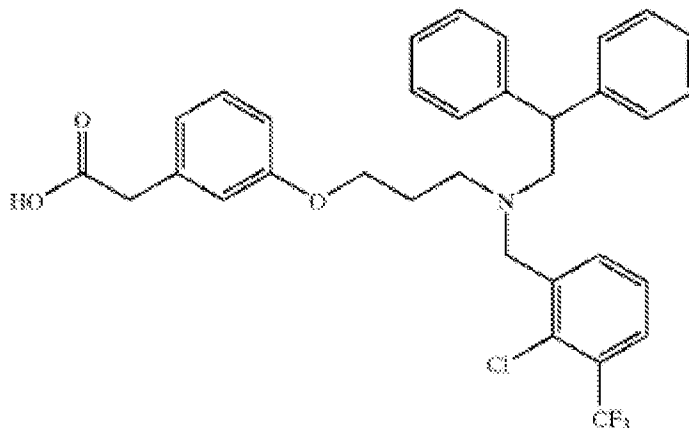
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al (US 2004/0072868).

Collins et al discloses the following compound as shown below (see col. 18, ex. 16):

EXAMPLE 16

[0315] 2-(3-{3-[[2-Chloro-3-(trifluoromethyl)benzyl](2,2-diphenylethyl)amino]propoxy}-phenyl)acetic Acid



However, the instant invention differs from the prior art in that the claimed moiety of the carboxylic acid is one or two carbons longer than that of the prior art compound.

Even so, compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ 425; *In re Druey*, 138 USPQ 39. In all of these cases, the close structural similarity

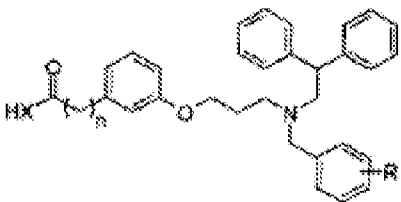


between two compounds differing by one or two methyl groups was itself sufficient show obviousness. See also MPEP 2144.09, second paragraph. Therefore, it would have been obvious to the skilled artisan in the art to be motivated to form its homologue as an alternative because the skilled artisan in the art would expect that homologues can be prepared by the same method and to have generally the same properties.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al (J. Med. Chem. 2002, 45, 1963-1966).

Collins et al discloses the following compound as shown below (see page 1964, Table 1 ):

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12	1	O	2-chloro-3-trifluoro- methyl methyl	125 ± 20	1.0	190 ± 30	1.7

However, the instant invention differs from the prior art in that the claimed moiety of the carboxylic acid is one or two carbons longer than that of the prior art compound.

Even so, compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing

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homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ 425; *In re Druey*, 138 USPQ 39. In all of these cases, the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. See also MPEP 2144.09, second paragraph. Therefore, it would have been obvious to the skilled artisan in the art to be motivated to form its homologue as an alternative because the skilled artisan in the art would expect that homologues can be prepared by the same method and to have generally the same properties.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Taylor Victor Oh, MSD,LAC  
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Art Unit : 1625

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6/11/08